

IN THE CLAIMS

Please amend the claims as follows.

1. (Currently amended) A composition comprising two or more isolated nucleic acids selected from the group consisting of an isolated nucleic acid encoding an *env* gene product or ~~an immunogenic fragment~~ a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product or ~~an immunogenic fragment~~ a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or ~~immunogenic~~ said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or ~~the immunogenic~~ said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or ~~an immunogenic fragment~~ a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or ~~immunogenic~~ said fragment thereof is modified to inhibit reverse transcriptase activity.

2. (Currently amended] A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or ~~immunogenic~~ said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or ~~the immunogenic~~ said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or ~~immunogenic~~ said fragment thereof is modified to inhibit reverse transcriptase activity, ~~and wherein the nucleic acids are each contained within a separate alphavirus replicon particle.~~

3. (Currently amended) A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1)

an isolated nucleic acid encoding an *env* gene product or ~~an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or ~~said immunogenic~~ fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or ~~said the immunogenic~~ fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or ~~immunogenic~~ said fragment thereof is modified to inhibit reverse transcriptase activity, and wherein ~~the nucleic acids are each contained within a separate alphavirus replicon particle, and further wherein~~ the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations.

4-10. (Canceled without prejudice)

11. (Previously presented) A method of inducing an immune response to human immunodeficiency virus in a subject, comprising administering to the subject an immunogenic amount of the composition of claim 1 in a pharmaceutically acceptable carrier.

12. (Previously presented) A method of inducing an immune response to human immunodeficiency virus in a subject, comprising administering to the subject an immunogenic amount of the composition of claim 2 in a pharmaceutically acceptable carrier.

13. (Previously presented) A method of inducing an immune response to human immunodeficiency virus in a subject, comprising administering to the subject an immunogenic amount of the composition of claim 3 in a pharmaceutically acceptable carrier.

14-20. (Canceled without prejudice)

21. (Currently amended) A composition comprising two or more isolated nucleic acids

selected from the group consisting of an isolated nucleic acid encoding an *env* gene product ~~an immunogenic fragment~~ a fragment containing an epitope thereof of a human immunodeficiency virus, an isolated nucleic acid encoding a *gag* gene product ~~an immunogenic fragment~~ a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *gag* gene product or ~~immunogenic~~ said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or ~~the immunogenic~~ said fragment thereof and their release from a cell, and an isolated nucleic acid encoding a *pol* gene product or ~~an immunogenic fragment~~ a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or ~~immunogenic~~ said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or ~~immunogenic~~ said fragment thereof.

22. (Currently amended) A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or ~~immunogenic~~ said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or the ~~immunogenic~~ said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or ~~immunogenic~~ said fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or ~~immunogenic~~ said fragment thereof, ~~and wherein the nucleic acids are each contained within a separate alphavirus replicon particle.~~

23. (Currently amended) A composition comprising a population of alphavirus replicon particles comprising two or more isolated nucleic acids selected from the group consisting of 1) an isolated nucleic acid encoding an *env* gene product, ~~or an immunogenic fragment~~ a fragment

containing an epitope thereof, of a human immunodeficiency virus, 2) an isolated nucleic acid encoding a *gag* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *gag* gene product or ~~immunogenic~~ said fragment thereof is modified to inhibit formation of virus-like particles containing the *gag* gene product or ~~the immunogenic~~ said fragment thereof and their release from a cell, and 3) an isolated nucleic acid encoding a *pol* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or ~~immunogenic~~ said fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or ~~immunogenic~~ said fragment thereof, and ~~wherein the nucleic acids are each contained within a separate alphavirus replicon particle, and further~~ wherein the alphavirus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations.

24-30. (Canceled without prejudice)

31. (Previously presented) A method of inducing an immune response to human immunodeficiency virus in a subject, comprising administering to the subject an immunogenic amount of the composition of claim 21 in a pharmaceutically acceptable carrier.

32. (Previously presented) A method of inducing an immune response to human immunodeficiency virus in a subject, comprising administering to the subject an immunogenic amount of the composition of claim 22 in a pharmaceutically acceptable carrier.

33. (Previously presented) A method of inducing an immune response to human immunodeficiency virus in a subject, comprising administering to the subject an immunogenic amount of the composition of claim 23 in a pharmaceutically acceptable carrier.

34-60. (Canceled without prejudice)

61. (Currently amended] An isolated nucleic acid encoding a *pol* gene product or ~~an immunogenic fragment~~ a fragment containing an epitope thereof of a human immunodeficiency virus, wherein the *pol* gene product or ~~immunogenic-said~~ fragment thereof comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the *pol* gene product or ~~immunogenic-said~~ fragment thereof.

62. (Previously presented) A composition comprising the nucleic acid of claim 61.

63. (Previously presented) A vector comprising the nucleic acid of claim 61.

64. (Previously presented) A cell comprising the vector of claim 63.

65. (Previously presented) An alphavirus replicon particle comprising the nucleic acid of claim 61.

66. (Currently amended} A method of making the alphavirus replicon particle of claim 65, comprising

a) providing a helper cell for producing an infectious, defective alphavirus particle, comprising in an alphavirus-permissive cell:

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- (i) an alphavirus replicon RNA, wherein the replicon RNA comprises an alphavirus packaging signal and a nucleic acid encoding a *pol* gene product, ~~or an immunogenic fragment~~ a fragment containing an epitope thereof, of a human immunodeficiency virus, wherein the *pol* gene product or ~~immunogenic-said~~ fragment thereof comprises a modification resulting in deletion or inactivation of protease, integrase, RNase H and reverse transcriptase functions in the *pol* gene product or ~~immunogenic-said~~ fragment thereof, and wherein the replicon RNA lacks sequences encoding alphavirus structural proteins;
 - (ii) a first helper RNA separate from said replicon RNA, said first helper RNA encoding at least one alphavirus structural protein and furthermore not encoding at least one other alphavirus structural protein; and

(iii) one or more additional helper RNA(s) separate from said replicon RNA and separate from said first helper RNA, said additional helper RNA(s) encoding at least one other alphavirus structural protein not encoded by said first helper RNA;

and with at least one of said helper RNAs lacking an alphavirus packaging signal;

wherein the combined expression of the alphavirus replicon RNA and the helper RNAs produces an assembled alphavirus replicon particle which is able to infect a cell, and is unable to complete viral ~~replication~~ propagation, and further wherein the population contains no detectable replication-competent alphavirus particles as determined by passage on permissive cells in culture;

(b) producing the alphavirus replicon particles in the helper cell; and

(c) collecting the alphavirus replicon particles from the helper cell.

67. (Previously presented) The method of claim 66, wherein at least one of said replicon RNA, said first helper RNA, and said one or more additional helper RNA(s) comprises one or more attenuating mutations.

68. (Previously presented) An alphavirus replicon particle produced according to the method of claim 66.

69. (Previously presented) An alphavirus replicon particle produced according to the method of claim 67.

70. (Previously presented) A method of inducing an immune response in a subject, comprising administering to the subject an immunogenic amount of the composition of claim 62 in a pharmaceutically acceptable carrier.

71. (Previously presented) A method of inducing an immune response in a subject, comprising administering to the subject an immunogenic amount of the alphavirus replicon particle of claim 65 in a pharmaceutically acceptable carrier.

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72-73. (Canceled without prejudice)

74. (Currently amended) A method of inducing an immune response in a subject, comprising administering to the subject an immunogenic amount of a composition comprising the alphavirus replicon particles of claim ~~65~~68 in a pharmaceutically acceptable carrier.

75. (Currently amended) A method of ~~treating or preventing infection by human immunodeficiency virus~~inducing an immune response in a subject, comprising administering to the subject an immunogenic amount of a composition comprising the alphavirus replicon particles of claim ~~65~~69 in a pharmaceutically acceptable carrier.
